60. **REMARKS**

Claims 31-32, 34-40, 42-49 and 53-59 currently appear in this application. The Office Action of May 20, 2005, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claim Objections

Claims 42-49 are objected to under 37 CFR 1.75 (c) as being of improper independent form for failing to further limit the subject matter of a previous claim.

Accordingly, claims 42-49 have been amended to recite a process.

Rejections under 35 U.S.C. 112

Claims 31-32, 34-40, 42-49 and 53-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is respectfully traversed. Claims 31, 39 and 55 have been amended in accordance with the Examiner's helpful suggestions.

Claim 31 has been corrected to recite "KP" rather than "PK", which stands for kilopond. Kilopond is the same as

kilogram force (kgf) and is broadly used for defining the hardness of tablets.

Art Rejections

Claims 31-32, 36 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley et al., hereinafter Holmes-Farley '754.

This rejection is respectfully traversed. In response to the amendment filed April 15, 2005 and the declaration filed March 1, 2005, the Examiner cites *In re Chupp*, 2 USPQ2d 1437 (Fed. Cir. 1987) as requiring the claims to be of the same scope as the declaration. It is respectfully submitted that a reading of *Chupp* shows that a declaration under 37 CFR 1.132 need not demonstrate that the claimed composition must be unexpectedly superior in **all** aspects to be unobvious. In this case, applicants demonstrated that tablets containing only the phosphate-binding polymer exhibited stickiness between tablets, and tablets containing HPC-L or HPMC exhibited stickiness. Tablets containing crystalline cellulose or L-HPC were not sticky. It should be noted that the hardness of the non-sticky tablets was lower than that for the tablets containing polymer-HPC-L. The hardness of 6.2 is not critical to an unexpectedly superior tablet, but rather the combination of particles of an average particle size of no more than 400

microns, at least 90% being particles no larger than 500 microns, and having a true specific gravity of 1.20-1.22 and a water content of 1-14%, and at least one of crystalline cellulose or substituted hydroxypropyl cellulose. It is this combination of factors plus a hardness of over 6.2 that produces an unexpectedly superior tablet. A tablet with this hardness, but without the other features claimed, would not possess these superior properties.

In the present case, it is the particular additive used, *i.e.*, crystalline cellulose or L-HPC that provides unexpectedly good effects. While the hardness of the tablet must be above 6 KP, this hardness is not critical because two to the tested tablets numbers 4 and 5, had hardness of 19.1 and 7.5 KP, respectively. The non-sticky tablets, on the other hand, had hardnesses of 8.6 and 7.4, respectively.

The Examiner concedes that the prior art does not teach the instant specific gravity and properties, and that Holmes-Farley '754 does not teach tablets. It is respectfully submitted that there is nothing in Holmes-Farley '754 that would lead one skilled in the art to prepare tablets containing the phosphate-binding polymers, because, as shown in the MATSUDA declaration, many tablet formulations of these phosphate-binding polymers are sticky and therefore are not useful as tablets because they are difficult to swallow. Even though Holmes-Farley '754 discloses that the compositions may

be in the form of tablets, the only dosage forms actually described are capsules. One skilled in the art reading Holmes-Farley '754 could not reasonably expect to achieve any success in formulating tablets having the desired physical properties that are achieved by the present invention. There is no motivation in Holmes-Farley '754 to prepare tablets containing the phosphate-binding polymer, and the MATSUDA declaration provides evidence that suitable tablets are only obtained with the particular additives used in the present invention.

Claims 34-35, 39-40, 42-46, 49 and 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley '754 in view of Chen et al.

This rejection is respectfully traversed. Chen's disclosure of microcrystalline cellulose and L-HPC as additives for levothyroxine has nothing to do with producing non-sticky tablets, because there is no indication that levothyroxine is sticky and has the same tablet formulating problems as does phosphate-binding polymer. Moreover, Chen teaches tabletting aids including HPC, HEC, L-HPC, and microcrystalline cellulose, and does not specify that one is better than the others. In fact, the MATSUDA declaration shows that HPC-L and HPMC produce sticky tablets, and there is nothing in Chen that would lead one skilled in the art to choose only crystalline cellulose or L-HPC.

There is no motivation to combine Holmes-Farley '754 with Chen, because Chen solves a problem different from that of the present invention, and Chen does not disclose or suggest that the microcrystalline or other celluloses are used so that tablets produced therefrom are not sticky.

As the Federal Circuit stated in *In re Lee*, 61 USPQ2d 1430 (January 18, 2002, Fed. Cir.), "As applied to the determination of patentability *vel non*, when the issue is obviousness, 'it is fundamental that rejections under 35 U.S.C. 103 must be based on evidence comprehended by the language of that section.' *In re Grasselli*, 53 USPQ2d 1769, 1774 (Fed. Cir. 2000)… When patentability turns on the question of obviousness, the search for an analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness *See, e.g., McGinley v. Franklin Sports, Inc*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ('the central question is whether there is a reason to combine [the] references,' a question of fact drawing on the *Graham* factors."

'The factual inquiry whether to combine references must be thorough and searching.' *Id*. This precedent has been reinforced in myriad decisions, and cannot be dispensed with, *See, e.g., Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000). ('a showing of a

suggestion, teaching, or motivation to combine the prior art references is an "essential component of an obviousness holding"') (quoting *C. R. Bard, Inc. v. M3 Systems, Inc.* 48 USPQ2d (Fed. Cir. 1998)) The Court went on to quote *In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999), "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."

There is a requirement for specificity in combining references, *See, In re Kotzab*, 55 USPQ2d 13134, 1317 (Fed. Cir. 2002)("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.").

In the present case, the Examiner has shown no motivation to combine Holmes-Farley '754 with Chen to produce a non-sticky tablet containing a phosphate-binding polymer.

Claims 37 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley '754 in view of Chen et al. and further in view of Nakajima.

This rejection is respectfully traversed. Nakajima adds nothing to Holmes-Farley '754 and Chen, because Nakajima merely discloses that stearic acid, magnesium stearate, and hydrogenated castor oil have been widely used in

pharmaceutical preparations. However, there is nothing in any of these cited patents that would lead one skilled in the art to produce a phosphate-binding polymer in tablet form. The MATSUDA declaration makes clear that only some conventional additives can be used to produce non-sticky tablets from phosphate-binding polymers. Nakajima adds nothing to Holmes-Farley '754 and Chen, because Nakajima does not teach or suggest that only certain additives can be used to make non-sticky tablets from phosphate-binding polymers.

Claims 31-32, 34, 36, 39-40, 42, 49 and 53-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley '754 in view of Yaginuma at al. or Battista.

This rejection is respectfully traversed. The Examiner concedes that the prior art cited does not teach the instant specific gravity and properties. However, despite Yaginuma's teaching that microcrystalline cellulose can be used to increase the strength of the tablet, this is not the reason the present invention uses microcrystalline cellulose. While Battista discloses that microcrystalline cellulose is less tacky and sticky than starch, there is nothing in either Yaginuma or Battista that suggests using microcrystalline cellulose with a phosphate-binding polymer would produce unexpectedly superior tablets. As noted above, it is not solely the hardness of the tablets that makes them superior. It is also the non-stickiness of the tablets that makes them

unusually superior, and only certain types of microcrystalline cellulose can be used to this effect. The MATSUDA declaration describes tackiness and hardness of several tablets made with crystalline cellulose. Only those made with crystalline cellulose and polymer L-HPC were not sticky. Tablets made with polymer HPC-L and HPMC were sticky.

Moreover, Battista discloses cellulose crystallite aggregates that have the capacity to adsorb and absorb moisture. Battista also discloses that under conditions of increasing humidity, for example, up to 85% relative humidity, starch becomes tacky and sticky whereas the aggregates do not (column 5, lines 66-74). The aggregates described in Battista are prepared from any of the neutral cellulose materials such as natural fibers, purified wood pulp, or regenerated forms of cellulose by the controlled acid hydrolysis of cellulose. The level-off D.P. value reflects a destruction of the original fibrous structure of the cellulosic source material (column 1, line 53 to column 2, line 35).

However, the aggregates of Battista differ from the crystalline cellulose used in the present invention. Battista discloses that tablets using the aggregates exhibit low disintegration (Example 6, column 11, lines 54-58). Therefore, one skilled in the art reading Battista would not be motivated to substitute the aggregates of Battista for

microcrystalline cellulose to obtain tablets with a degree of hardness greater than 6KP.

Claims 35, 37-38, and 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes-Farley et al. in view of Yaginuma et al. or Battista further in view of Sato et al.

This rejection is respectfully traversed. Sato never discloses that the succinic acid compounds are sticky when formulated into tablets, so there is no teaching or suggestion for specifically using L-HPC rather than other cellulose compounds to prevent the tablets from becoming sticky and difficult to swallow.

The present invention provides tablets having a hardness of 6.2 KP or greater comprising particles of a phosphate-binding polymer having an average particle size of no more than 400 microns, with at least 90% being occupied by particles no larger than 500 microns, and heaving a true specific gravity of 1.20-1.22 and a water content of 1-14%, and at least one of crystalline cellulose or low substituted hydroxypropyl cellulose. None of the patents cited, alone or in combination, would suggest to one skilled in the art that tablets can be prepared from this particular combination of ingredients having the specific physical characteristics recited.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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